

&lt;110&gt; NATSPEARS LTD.

&lt;120&gt; NK CELL RECEPTOR CONJUGATES FOR TREATING MALIGNANCIES

&lt;130&gt; NAP002-PCT

&lt;150&gt; US 60/431,728

&lt;151&gt; 2002-12-09

&lt;160&gt; 14

&lt;170&gt; PatentIn version 3.1

&lt;210&gt; 1

&lt;211&gt; 488

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 1

Met Ser Ser Thr Leu Pro Ala Leu Leu Cys Val Gly Leu Cys Leu Ser  
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Gln Arg Ile Ser Ala Gln Gln Gln Thr Leu Pro Lys Pro Phe Ile Trp  
 20 25 30

Ala Glu Pro His Phe Met Val Pro Lys Glu Lys Gln Val Thr Ile Cys  
 35 40 45

Cys Gln Gly Asn Tyr Gly Ala Val Glu Tyr Gln Leu His Phe Glu Gly  
 50 55 60

Ser Leu Phe Ala Val Asp Arg Pro Lys Pro Pro Glu Arg Ile Asn Lys  
 65 70 75 80

Val Lys Phe Tyr Ile Pro Asp Met Asn Ser Arg Met Ala Gly Gln Tyr  
 85 90 95

Ser Cys Ile Tyr Arg Val Gly Glu Leu Trp Ser Glu Pro Ser Asn Leu  
 100 105 110

Leu Asp Leu Val Val Thr Glu Met Tyr Asp Thr Pro Thr Leu Ser Val  
 115 120 125

His Pro Gly Pro Glu Val Ile Ser Gly Glu Lys Val Thr Phe Tyr Cys  
 130 135 140

Arg Leu Asp Thr Ala Thr Ser Met Phe Leu Leu Leu Lys Glu Gly Arg  
 145 150 155 160

Ser Ser His Val Gln Arg Gly Tyr Gly Lys Val Gln Ala Glu Phe Pro  
 165 170 175

Leu Gly Pro Val Thr Thr Ala His Arg Gly Thr Tyr Arg Cys Phe Gly  
 180 185 190

Ser Tyr Asn Asn His Ala Trp Ser Phe Pro Ser Glu Pro Val Lys Leu  
 195 200 205

Leu Val Thr Gly Asp Ile Glu Asn Thr Ser Leu Ala Pro Glu Asp Pro  
 210 215 220  
 Thr Phe Pro Ala Asp Thr Trp Gly Thr Tyr Leu Leu Thr Thr Glu Thr  
 225 230 235 240  
 Gly Leu Gln Lys Asp His Ala Leu Trp Asp His Thr Ala Gln Asp Pro  
 245 250 255  
 Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala  
 260 265 270  
 Pro Glu Phe Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
 275 280 285  
 Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
 290 295 300  
 Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val  
 305 310 315 320  
 Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
 325 330 335  
 Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
 340 345 350  
 Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala  
 355 360 365  
 Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
 370 375 380  
 Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr  
 385 390 395 400  
 Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
 405 410 415  
 Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
 420 425 430  
 Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
 435 440 445  
 Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe  
 450 455 460  
 Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys  
 465 470 475 480  
 Ser Leu Ser Leu Ser Pro Gly Lys  
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<210> 2  
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 <212> PRT  
 <213> Homo sapiens

<400> 2

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Leu Gly Met Leu Val Ala Ser Cys Leu Gly Arg Leu Arg Val Pro Gln
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Gln Gln Thr Leu Pro Lys Pro Phe Ile Trp Ala Glu Pro His Phe Met
35          40          45

Val Pro Lys Glu Lys Gln Val Thr Ile Cys Cys Gln Gly Asn Tyr Gly
50          55          60

Ala Val Glu Tyr Gln Leu His Phe Glu Gly Ser Leu Phe Ala Val Asp
65          70          75          80

Arg Pro Lys Pro Pro Glu Arg Ile Asn Lys Val Lys Phe Tyr Ile Pro
85          90          95

Asp Met Asn Ser Arg Met Ala Gly Gln Tyr Ser Cys Ile Tyr Arg Val
100         105         110

Gly Glu Leu Trp Ser Glu Pro Ser Asn Leu Leu Asp Leu Val Val Thr
115         120         125

Glu Met Asp Pro Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
130         135         140

Pro Cys Pro Ala Pro Glu Phe Glu Gly Ala Pro Ser Val Phe Leu Phe
145         150         155         160

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
165         170         175

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
180         185         190

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
195         200         205

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
210         215         220

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
225         230         235         240

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
245         250         255

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Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg  
260 265 270

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly  
275 280 285

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro  
290 295 300

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser  
305 310 315 320

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln  
325 330 335

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His  
340 345 350

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
355 360

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<213> Homo sapiens

<400> 3

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Leu Gly Met Leu Val Ala Ser Cys Leu Gly Arg Leu Arg Val Pro Tyr  
20 25 30

Asp Thr Pro Thr Leu Ser Val His Pro Gly Pro Glu Val Ile Ser Gly  
35 40 45

Glu Lys Val Thr Phe Tyr Cys Arg Leu Asp Thr Ala Thr Ser Met Phe  
50 55 60

Leu Leu Leu Lys Glu Gly Arg Ser Ser His Val Gln Arg Gly Tyr Gly  
65 70 75 80

Lys Val Gln Ala Glu Phe Pro Leu Gly Pro Val Thr Thr Ala His Arg  
85 90 95

Gly Thr Tyr Arg Cys Phe Gly Ser Tyr Asn Asn His Ala Trp Ser Phe  
100 105 110

Pro Ser Glu Pro Val Lys Leu Leu Val Thr Gly Asp Ile Glu Asn Thr  
115 120 125

Ser Leu Ala Pro Glu Asp Pro Thr Phe Pro Asp Thr Trp Gly Thr Tyr  
130 135 140

Leu Leu Thr Thr Glu Thr Gly Leu Gln Lys Asp His Ala Leu Trp Asp  
145 150 155 160

Pro Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro  
165 170 175

Ala Pro Glu Phe Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys  
180 185 190

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val  
195 200 205

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr  
210 215 220

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu  
225 230 235 240

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His  
245 250 255

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys  
260 265 270

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln  
275 280 285

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu  
290 295 300

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro  
305 310 315 320

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn  
325 330 335

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu  
340 345 350

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val  
355 360 365

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln  
370 375 380

Lys Ser Leu Ser Leu Ser Pro Gly Lys  
385 390

<210> 4  
<211> 382  
<212> PRT  
<213> Homo sapiens

<400> 4

Met Gly Met Pro Met Gly Ser Leu Gln Pro Leu Ala Thr Leu Tyr Leu

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Leu Gly Met	Leu Val Ala Ser Cys	Leu Gly Arg Leu Arg Val	Pro Leu
	20	25	30
Trp Val	Ser Gln Pro Leu Glu Ile Arg Thr Leu Glu Gly	Ser Ser Ala	
	35	40	45
Phe Leu Pro Cys Ser Phe Asn Ala Ser Gln Gly Arg Leu Ala Ile Gly			
50	55	60	
Ser Val Thr Trp Phe Arg Asp Glu Val Val Pro Gly Lys Glu Val Arg			
65	70	75	80
Asn Gly Thr Pro Glu Phe Arg Gly Arg Leu Ala Pro Leu Ala Ser Ser			
	85	90	95
Arg Phe Leu His Asp His Gln Ala Glu Leu His Ile Arg Asp Val Arg			
	100	105	110
Gly His Asp Ala Ser Ile Tyr Val Cys Arg Val Glu Val Leu Gly Leu			
	115	120	125
Gly Val Gly Thr Gly Asn Gly Thr Arg Leu Val Val Glu Lys Glu His			
	130	135	140
Pro Gln Leu Gly Asp Pro Glu Pro Lys Ser Ser Asp Lys Thr His Thr			
145	150	155	160
Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Ala Pro Ser Val Phe			
	165	170	175
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro			
	180	185	190
Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val			
	195	200	205
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr			
	210	215	220
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val			
225	230	235	240
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys			
	245	250	255
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser			
	260	265	270
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro			
	275	280	285
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val			

290

295

300

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly  
 305 310 315 320

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp  
 325 330 335

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp  
 340 345 350

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His  
 355 360 365

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys  
 370 375 380

<210> 5  
 <211> 434  
 <212> PRT  
 <213> Homo sapiens

<400> 5

Met Gly Met Pro Met Gly Ser Leu Gln Pro Leu Ala Thr Leu Tyr Leu  
 1 5 10 15

Leu Gly Met Leu Val Ala Ser Cys Leu Gly Arg Leu Arg Val Pro Gln  
 20 25 30

Ser Lys Ala Gln Val Leu Gln Ser Val Ala Gly Gln Thr Leu Thr Val  
 35 40 45

Arg Cys Gln Tyr Pro Pro Thr Gly Ser Leu Tyr Glu Lys Lys Gly Trp  
 50 55 60

Cys Lys Glu Ala Ser Ala Leu Val Cys Ile Arg Leu Val Thr Ser Ser  
 65 70 75 80

Lys Pro Arg Thr Val Ala Trp Thr Ser Arg Phe Thr Ile Trp Asp Asp  
 85 90 95

Pro Asp Ala Gly Phe Phe Thr Val Thr Met Thr Asp Leu Arg Glu Glu  
 100 105 110

Asp Ser Gly His Tyr Trp Cys Arg Ile Tyr Arg Pro Ser Asp Asn Ser  
 115 120 125

Val Ser Lys Ser Val Arg Phe Tyr Leu Val Val Ser Pro Ala Ser Ala  
 130 135 140

Ser Thr Gln Thr Ser Trp Thr Pro Arg Asp Leu Val Ser Ser Gln Thr  
 145 150 155 160

Gln Thr Gln Ser Cys Val Pro Pro Thr Ala Gly Ala Arg Gln Ala Pro  
 165 170 175

Glu Ser Pro Ser Thr Ile Pro Val Pro Ser Gln Pro Gln Asn Ser Thr  
 180 185 190  
 Leu Arg Pro Gly Pro Ala Ala Pro Asp Pro Glu Pro Lys Ser Ser Asp  
 195 200 205  
 Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Phe Glu Gly Ala  
 210 215 220  
 Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile  
 225 230 235 240  
 Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu  
 245 250 255  
 Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His  
 260 265 270  
 Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg  
 275 280 285  
 Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys  
 290 295 300  
 Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu  
 305 310 315 320  
 Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr  
 325 330 335  
 Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu  
 340 345 350  
 Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp  
 355 360 365  
 Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val  
 370 375 380  
 Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp  
 385 390 395 400  
 Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His  
 405 410 415  
 Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro  
 420 425 430  
 Gly Lys

<210> 6  
 <211> 326



&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 6

Met Gly Met Pro Met Gly Ser Leu Gln Pro Leu Ala Thr Leu Tyr Leu  
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Leu Gly Met Leu Val Ala Ser Cys Leu Gly Arg Leu Arg Val Pro Ser  
 20 25 30

Pro Ala Ser Ala Ser Thr Gln Thr Ser Trp Thr Pro Arg Asp Leu Val  
 35 40 45

Ser Ser Gln Thr Gln Thr Gln Ser Cys Val Pro Pro Thr Ala Gly Ala  
 50 55 60

Arg Gln Ala Pro Glu Ser Pro Ser Thr Ile Pro Val Pro Ser Gln Pro  
 65 70 75 80

Gln Asn Ser Thr Leu Arg Pro Gly Pro Ala Ala Pro Asp Pro Glu Pro  
 85 90 95

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu  
 100 105 110

Phe Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp  
 115 120 125

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp  
 130 135 140

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly  
 145 150 155 160

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn  
 165 170 175

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp  
 180 185 190

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro  
 195 200 205

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu  
 210 215 220

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn  
 225 230 235 240

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile  
 245 250 255

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr  
 260 265 270

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys  
 275 280 285

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys  
 290 295 300

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu  
 305 310 315 320

Ser Leu Ser Pro Gly Lys  
 325

<210> 7  
 <211> 376  
 <212> PRT  
 <213> Homo sapiens

<400> 7

Met Gly Met Pro Met Gly Ser Phe Gln Pro Leu Ala Thr Leu Tyr Leu  
 1 5 10 15

Leu Gly Met Leu Val Ala Ser Cys Leu Gly Arg Leu Arg Val Pro Gln  
 20 25 30

Ser Lys Ala Gln Val Leu Gln Ser Val Ala Gly Gln Thr Leu Thr Val  
 35 40 45

Arg Cys Gln Tyr Pro Pro Thr Gly Ser Leu Tyr Glu Lys Lys Gly Trp  
 50 55 60

Cys Lys Glu Ala Ser Ala Leu Val Cys Ile Arg Leu Val Thr Ser Ser  
 65 70 75 80

Lys Pro Arg Thr Val Ala Trp Thr Ser Arg Phe Thr Ile Trp Asp Asp  
 85 90 95

Pro Asp Ala Gly Phe Phe Thr Val Thr Met Thr Asp Leu Arg Glu Glu  
 100 105 110

Asp Ser Gly His Tyr Trp Cys Arg Ile Tyr Arg Pro Ser Asp Asn Ser  
 115 120 125

Val Ser Lys Ser Val Arg Phe Tyr Leu Val Val Ser Pro Ala Asp Pro  
 130 135 140

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala  
 145 150 155 160

Pro Glu Phe Glu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
 165 170 175

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
 180 185 190

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val  
195 200 205

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
210 215 220

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
225 230 235 240

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala  
245 250 255

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
260 265 270

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr  
275 280 285

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
290 295 300

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
305 310 315 320

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
325 330 335

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe  
340 345 350

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys  
355 360 365

Ser Leu Ser Leu Ser Pro Gly Lys  
370 375

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<212> DNA  
<213> Homo sapiens

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 <212> DNA  
 <213> Homo sapiens

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ctttttgccg	tggacagacc aaaacccctt gagcggatta acaaagtcaa attctacatc 300
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 <211> 1197  
 <212> DNA  
 <213> Homo sapiens

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 <211> 1164  
 <212> DNA  
 <213> Homo sapiens

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 cagccccttg agattcgtac cctggaaggg tcttctgcct tctgcccctg ctccttcaat 180  
 gccagccaag ggagactggc cattgggtcc gtcacgtggt tccgagatga ggtggttcca 240  
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